REMARKS

The claims have been amended to place them in a format more customary to US patent practice. No new matter has been added.

Information Disclosure Statement

A replacement form PTO-1449 is enclosed. The replacement sheet contains the inventors names for items 3-6 on PTO-1449. Applicants' respectfully request the Examiner to initial form 1449 indicating that reference items 3-6 have been considered. Citations 7-10 are equivalent to citations 3-6 as previously noted.

Replacement Drawings

A replacement drawing sheet is attached which includes the appropriate SEQ ID No. on figures 8-A (i.e., SEQ ID No. 1) and 8-B (i.e, SEQ ID No 2).

Claim Objections

Claims 3 and 22 have been amended to include the SEQ ID Nos. Thus, it is respectfully requested that the claim objections be withdrawn.

Rejections under 35 USC 101 and 112

Claims 1-4, 7, and 8 are rejected under 35 U.S.C. § 101 and §112.
The "use" claims have been amended to place them in a format more customary to US patent practice.

It is believed that the amendments to the claims render the rejection moot. Thus, it is respectfully requested that the rejections be withdrawn.

Rejections under 35 U.S.C. 102(b)

Claims 9-10, and 22 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Aruffo et al., (US Patent 6,210,669). Claims 9-11, and 22 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Kim et al., (Cancer Research, Vol 61, page

2031-2037, 2001). Applicants' respectfully traverse the rejections.

Neither, Aruffo et al. nor Kim et al. disclose antagonistic CD137 antibodies. They both disclose agonistic antibodies against CD137. For example, page 2032, right column, first and second line, of Kim et at, states:

> 1D8 and 3E1 anti-41BB mAbs, both of which are of rat origin and bind and activate murine 4-1BB receptor, were generously supplied by Bristol-Myers Squibb.

Furthermore, as noted above, the antibodies (1D8 and 3E1) were supplied by Bristol-Myers Squibb and are the same antibodies as mentioned in Aruffo et al. (US 6,210,669 Bristol-Myers Squibb).

Thus, both Aruffo et al, and Kim et al. disclose the use of agonistic CD137 antibodies for the treatment of tumors and not an antagonist antibody to CD 137 for the treatment of tumors.

Furthermore, on page 6 of the Office Action the Examiner alleges that the burden is on the Applicants to prove that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. However, the burden has not shifted. The Examiner has provided no reasonable reasons or evidence to establish that the prior art agonist is actually an antagonist, the opposite.

Thus, based on the above remarks it is respectfully requested that the rejections under 35 USC §102 be withdrawn.

Rejections under 35 USC 103

Claims 9, 11, and 12 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Aruffo et al., (US Patent 6,210,669) or Kim et al., (Cancer Research, vol 169, page 1792-1800, Aug. 2002). Claims 1-4, 7-12, 22 and 23 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Kwon B. (US Patent 6,303,121) in view of Broil et

al., (Am J Clin Pathol, Col 115 page, 543-549, 2001) or Schwarz et al (Blood, vol 85, page 1043-1052, 1995). The rejections are respectfully traversed.

Both Aruffo et al, and Kim et al., discussed above, disclose the use of agonistic CD137 antibodies for the treatment of tumors and not antagonist CD137 antibodies for the treatment of tumors. Thus, they could not possibly render the use of an antagonist CD137 antibody obvious.

Kwon (US 6,303,121) discloses CD137 agonistic antibodies BBK-1 and BBK-4. Additionally, Kwon discloses the antagonist antibodies BBK-2 and BBK-3. However, as can be seen in column 5, lines 22 to 59, it is the agonistic antibodies that are used for the treatment of tumors (due to a general stimulation of the immune system through amplification of T cell proliferation and T-cell activation, respectively). In contrast, Kwon teaches that the antagonistic antibodies are useful for the suppression of immune reactions (see col. 5, lines 32-34).

Thus, Kwon et at, teaches a skilled worker to use CD137 agonists for the treatment of tumors (such as B-cell lymphoma). Kwon does not teach or suggest the use of antagonistic molecule against CD137 for the treatment of tumors. The last line of the Kwon abstract does not change this summary. It does not disclose agonists for treating cancer. Overall, the primary references (Kwon, Aruffo et al, and Kim et al.) are perfectly consistent. Only agonists are disclosed for treating tumors.

Even if Broil et. al. and Schwarz et al. did teach CD137 expression on cancer cells there is nothing that would lead a skilled worker to choose an antagonist antibody for the treatment of tumors expressing CD137. This is especially true since all the primary references teach a skilled worker to choose a CD137 agonist antibody.

In any event, the Examiner alleges that Broil et at. shows that CD137 is expressed on activated hematopoietic cells and B-cell lymphoma cells, respectively. However, Broil et. al. does not show that CD137 is expressed on tumor cells as alleged. Broil et al. shows CD137 expression on the blood vessels of tumors (see, for

example, the title of Broil et al. - *CD137 Expression in Tumor Vessel Walls*) and not the tumor cells themselves. A skilled worker would recognize that blood vessel walls and tumor cells are not the same.

Thus, based on the above remarks it is respectfully requested that the rejections under 35 USC §103 be withdrawn.

With regards to the election of species, in accordance with M.P.E.P. §803.02, the Examiner is reminded that, should no prior art be found which renders the invention of the elected species (i.e., B cell lymphoma and Antibody BBK-2) unpatentable, the search of the remainder of the generic claim(s) should be continued in the same application. It is improper for the PTO to refuse to examine in one application the entire scope of the claims therein unless they lack unity of invention.

If any issues remain, applicants request that the Examiner contact the undersigned by telephone to expeditiously resolve any outstanding issues.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,
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